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PATENT  
Attorney Docket No.: 020130-000111US

Assistant Commissioner for Patents  
Washington, D.C. 20231

On 3 Sept. 2002

TOWNSEND and TOWNSEND and CREW LLP

By: Malinda O'Neil

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

WANG et al.

Application No.: 09/870,353

Filed: May 30, 2001

For: IMPROVED NUCLEIC ACID  
MODIFYING ENZYMES

Examiner: Not yet assigned

Art Unit: 1633

SUPPLEMENTAL INFORMATION  
DISCLOSURE STATEMENT UNDER 37  
CFR §1.97 and §1.98

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

The reference cited on attached form PTO/SB/08B is being called to the attention of the Examiner. A copy of the reference is enclosed. This reference has been newly cited by the examining authority in the corresponding PCT application. A copy of the relevant part of the Written Opinion is enclosed. It is respectfully requested that the cited reference be expressly considered during the prosecution of this application, and the reference be made of record therein and appear among the "references cited" on any patent to issue therefrom.

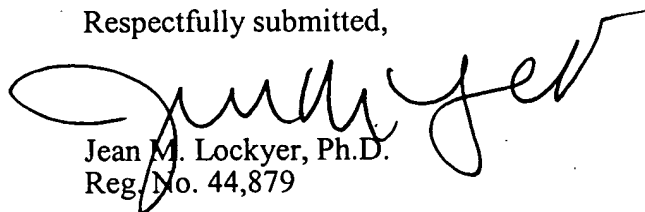
As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no

representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

Applicant believes that no fee is required for submission of this statement.

However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Jean M. Lockyer', is written over the typed name and registration number.

Jean M. Lockyer, Ph.D.  
Reg. No. 44,879

TOWNSEND and TOWNSEND and CREW LLP  
Two Embarcadero Center, 8<sup>th</sup> Floor  
San Francisco, California 94111-3834  
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JML:mcd  
Unsaved Document

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO  <h2 style="text-align: center; margin: 10px 0;">INFORMATION DISCLOSURE STATEMENT BY APPLICANT</h2> <p style="text-align: center; margin-top: 20px;"><i>(use as many sheets as necessary)</i></p>		<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <th colspan="2" style="text-align: right; padding: 5px;"><b>Complete If Known</b></th> </tr> <tr> <td style="width: 35%; padding: 5px;">Application Number</td> <td style="padding: 5px;">09/870,353</td> </tr> <tr> <td style="padding: 5px;">Filing Date</td> <td style="padding: 5px;">May 30, 2001</td> </tr> <tr> <td style="padding: 5px;">First Named Inventor</td> <td style="padding: 5px;">Wang, Yan, et. al.</td> </tr> <tr> <td style="padding: 5px;">Art Unit</td> <td style="padding: 5px;">1633</td> </tr> <tr> <td style="padding: 5px;">Examiner Name</td> <td style="padding: 5px;">Not yet assigned</td> </tr> <tr> <td style="padding: 5px;">Attorney Docket Number</td> <td style="padding: 5px;">020130-000111US</td> </tr> </table>		<b>Complete If Known</b>		Application Number	09/870,353	Filing Date	May 30, 2001	First Named Inventor	Wang, Yan, et. al.	Art Unit	1633	Examiner Name	Not yet assigned	Attorney Docket Number	020130-000111US
<b>Complete If Known</b>																	
Application Number	09/870,353																
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First Named Inventor	Wang, Yan, et. al.																
Art Unit	1633																
Examiner Name	Not yet assigned																
Attorney Docket Number	020130-000111US																

[illegible]

Examiner Signature		Date Considered	
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\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

**Burden Hour Statement:** This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO:** Assistant Commissioner for Patents, Washington, DC 20231.

WRITTEN OPINION

International application No.  
PCT/US01/17492

**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. STATEMENT**

Novelty (N)	Claims <u>3-5, 7-23, 26-28 and 30-44</u>	YES
	Claims <u>1, 2, 6, 24, 25 and 29</u>	NO
Inventive Step (IS)	Claims <u>3-5, 7-23, 26-28 and 30-44</u>	YES
	Claims <u>1, 2, 6, 24, 25 and 29</u>	NO
Industrial Applicability (IA)	Claims <u>1-44</u>	YES
	Claims <u>NONE</u>	NO

**2. CITATIONS AND EXPLANATIONS**

Claims 1, 2, 6, 24, 25 and 29 lack novelty under PCT Article 33(2) as being anticipated by CARRODEGUAS et al. CARRODEGUAS et al. teach the cloning of the cDNA which encodes the accessory subunit of *Xenopus laevis* mitochondrial DNA (mtDNA) polymerase  $\gamma$  (pol  $\gamma$ ) and teach that the *Xenopus* accessory subunit  $\gamma$ B binds to the human  $\gamma$ A catalytic subunit and this association of the *Xenopus* accessory subunit with human  $\gamma$ A increased the processivity of the  $\gamma$ A catalytic subunit relative to the same protein in the absence of the *Xenopus*  $\gamma$ B subunit. CARRODEGUAS et al. teach the ability of the *Xenopus*  $\gamma$ B subunit to increase the processivity of the human  $\gamma$ A catalytic subunit using an assay/method of modifying a nucleic acid in an aqueous solution by contacting the nucleic acid with the heterologous protein subunits and permitting the catalytic subunit to modify the nucleic acid solution.

Claims 3-5, 7-23, 26-28 and 30-44 meet the criteria set out in PCT Article 33(2)-(3) because the prior art does not teach or fairly suggest the claimed invention.

---NEW CITATIONS---

CARRODEGUAS et al. The Accessory Subunit of *Xenopus laevis* Mitochondrial DNA Polymerase gamma Increases Processivity of the Catalytic Subunit of Human DNA Polymerase gamma and Is Related to Class II Aminoacyl-tRNA Synthetases. *Molecular and Cellular Biology*. June 1999, Vol. 19, No. 6, pages 4039-4046. See entire document especially page 4043.

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PATENT  
Attorney Docket No.: 020130-000111US

Assistant Commissioner for Patents  
Washington, D.C. 20231

On 10/18/01

TOWNSEND and TOWNSEND and CREW LLP

By: 

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Yan Wang, Lei Xi and Dennis E. Prosen

Application No.: 09/870,353

Filed: May 30, 2001

For: IMPROVED NUCLEIC ACID  
MODIFYING ENZYMES

Examiner:

Art Unit: 1633

INFORMATION DISCLOSURE  
STATEMENT UNDER 37 CFR §1.97 and  
§1.98

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

The references cited on attached form PTO/SB/08A and PTO/SB/08B are being called to the attention of the Examiner. Copies of the references are enclosed. Also enclosed is a copy of the International Search Report from the corresponding PCT application. It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no

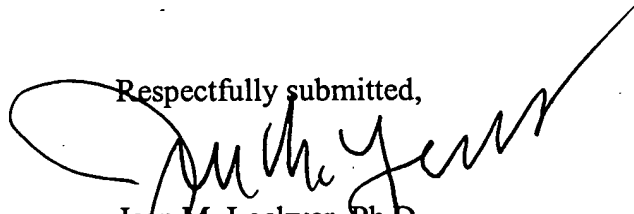
representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

CERTIFICATION

I hereby certify that no item of information in the information disclosure statement filed herewith was cited in a communication from a foreign patent office in a counterpart foreign application or, to my knowledge after making reasonable inquiry, was known to any individual designated in Section 1.56(c) more than three months prior to the filing of this information disclosure statement.

Applicant believes that no fee is required for submission of this statement, since it is being submitted prior to the first Office Action on the merits. However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,



Jean M. Lockyer, Ph.D.  
Reg. No. 44,879

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U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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Substitute for form 1448A/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	09/870,353
				Filing Date	May 30, 2001
				First Named Inventor	Wang, Yan
				Group Art Unit	1633
				Examiner Name	
Sheet	1	of	3	Attorney Docket Number	020130-000111US

U.S. PATENT DOCUMENTS						
Examiner Initials *	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
	AA	5,474,911	A	Pontius, <i>et al.</i>	12-12-1995	
	AB	5,972,603	A	Bedford, <i>et al.</i>	10-26-1999	
	AC	6,228,628	B1	Gelfand, <i>et al.</i>	05-08-2001	

Examiner Signature		Date Considered	
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\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

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Substitute for form 1449B/PTO

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 2 of 3

### Complete if Known

Application Number	09/870,353
Filing Date	May 30, 2001
First Named Inventor	Wang, Yan
Group Art Unit	1633
Examiner Name	
Attorney Docket Number	020130-000111US

### OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	AD	Baumann <i>et al.</i> , "Solution Structure and DNA-binding Properties of a Thermostable Protein from the Archaeon <i>Sulfolobus solfataricus</i> " <i>Structural Biology</i> (1994) Vol. 1(11), pp. 808-819.	
	AE	Bedford, <i>et al.</i> "The Thioredoxin Binding Domain of Bacteriophage T7 DNA Polymerase Confers Processivity on Escherichia coli DNA Polymerase I" <i>Proc. Natl. Acad. Sci. USA</i> (January 1997) Vol. 94, pp. 479-484.	
	AF	Cann <i>et al.</i> , "Functional Interactions of a Homolog of Proliferating Cell Nuclear Antigen with DNA Polymerases in Archaea," <i>Journal of Bacteriology</i> (1999) Vol. 181(21), pp. 6591-6599.	
	AG	Choli <i>et al.</i> , "Isolation, Characterization and Microsequence Analysis of a Small Basic Methylated DNA-binding Protein from the Archaeobacterium, <i>Sulfolobus solfataricus</i> " <i>Biochimica et Biophysica Acta</i> (1988) Vol. 950, pp. 193-203.	
	AH	De Felice <i>et al.</i> , "Two DNA polymerase Sliding Clamps from the Thermophilic Archaeon <i>Sulfolobus solfataricus</i> " <i>J. Molec. Biol.</i> (1999) Vol. 291, pp. 47-57.	
	AI	Gao <i>et al.</i> , "The Crystal Structure of the Hyperthermophile Chromosomal Protein Sso7d Bound to DNA" <i>Nature Structural Biology</i> (1998) Vol. 5(9), pp. 782-786.	
	AJ	Lim, <i>et al.</i> "The Mitochondrial p55 Accessory Subunit of Human DNA Polymerase $\gamma$ Enhances DNA Binding, Promotes Processive DNA Synthesis, and Confers N-Ethylmaleimide Resistance" <i>J. Biological Chemistry</i> (December 1999) Vol. 274(53), pp. 38197-38203.	
	AK	McAfee, <i>et al.</i> , "Gene Cloning, Expression, and Characterization of the Sac7 Proteins From the Hyperthermophile <i>Sulfolobus acidocaldarius</i> " <i>Biochemistry</i> (1995) Vol. 34, pp. 10063-10077.	
	AL	Sandman, <i>et al.</i> , "Histone-encoding Genes from <i>Pyrococcus</i> : Evidence for Members of the HMf Family of Archaeal Histones in a Non-methanogenic Archaeon" <i>Gene</i> (1994) Vol. 150, pp. 207-208.	
	AM	Shamoo, <i>et al.</i> "Building a Replisome from Interacting Pieces: Sliding Clamp Complexed to a Peptide from DNA Polymerase and a Polymerase Editing Complex" <i>Cell</i> (1999) Vol. 99, pp. 155-166.	

Examiner  
Signature

Date  
Considered

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			Application Number	09/870,353	
			Filing Date	May 30, 2001	
			First Named Inventor	Wang, Yan	
			Group Art Unit	1633	
			Examiner Name		
Sheet	3	of	3	Attorney Docket Number	020130-000111US

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS				
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.		T <sup>2</sup>
	AN	Starich, <i>et al.</i> , "NMR Structure of HMfB from the Hyperthermophile, <i>Methanothermus fervidus</i> , Confirms that this Archaeal Protein is a Histone" <i>J. Molec. Biol.</i> (1996) Vol. 255 pp. 187-203.		
	AO	Zhang <i>et al.</i> , "Expression and Psysicochemical Characterization of Human Proliferating Cell Nuclear Antigen" <i>Biochemistry</i> (1995) Vol. 34, pp. 10703-10712.		

Examiner Signature		Date Considered	
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SF 1280465 v1

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/17492

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(7) : C12N 9/12; C12Q 1/68, 1/48; C12P 19/34; C07K 14/00, 1/00 US CL : 435/194, 6, 15, 91.1; 530/300, 324, 350 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/194, 6, 15, 91.1; 530/300, 324, 350  Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,972,603 A (BEDFORD et al) 26 October 1999 (26.10.1999), see entire document.	1-44
Y	BEDFORD et al., The thioredoxin binding domain of bacteriophage T7DNA polymerase confers processivity on Escherichia coli DNA polymerase I. Proc. Natl. Acad. Sci. USA. January 1997, Vol. 94, pages 479-484, see entire document.	1-44
Y	LIM et al. The Mitochondrial p55 Accessory Subunit of Human DNA Polymerase g Enhances DNA Binding, Promotes Processive DNA Synthesis, and Confers N-Ethylmaleimide Resistance. J. Biological Chemistry. 31 December 1999, Vol. 274, No. 53, pages 38197-38203, see entire document.	1-44
Y, P	US 6,228,628 B1 (GELFAND et al) 08 May 2001 (08.05.2001) see entire document.	1-44
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 02 August 2001 (02.08.2001)		Date of mailing of the international search report 24 AUG 2001
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230		Authorized officer Richard Hutson Telephone No. (703) 308-0196